AMENDMENT TO THE CLAIMS

1. (Original) A compound for modulating kinase activity of Formula I,

or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

Ar is a five- to six-membered aromatic ring system containing between one and three heteroatoms, said five- to six-membered aromatic ring system substituted with -X and -Y-L-Z, in an ortho relationship to each other, and said five- to six-membered aromatic ring system optionally substituted with up to four R¹;

each R^1 is independently selected from -H, halogen, -CN, -NO₂, -OR³, -N(R³)R³, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, -OC(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower heterocyclylalkyl;

optionally two of R¹, together with the atoms to which they are attached, form a first ring system fused with Ar, said first ring system substituted with zero to three additional of R¹;

X is selected from the following six formulae:

wherein,

W is selected from $-C(R^2)(R^2)$ -, $-N(R^4)$ -, $-S(O)_{0-2}$ -, and -O-;

n = 1 or 2;

p = 0 or 1;

q is 1 to 3;

M is $-OR^3$ or $-N(R^3)R^4$;

each R^2 is independently selected from -H, halogen, oxo, -CN, -NH₂, -NO₂, -OR³, -N(R³)R³, -N(R³)R⁵, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -N(R³)C(O)N(R³)R³, -C(O)R³, -OC(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower heterocyclylalkyl;

two of R², together with the atoms to which they are attached, can form an optionally substituted three- to seven-membered ring system;

each R³ is independently selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; or

two of R³, when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl ring, said optionally substituted five- to seven-membered heterocyclyl ring optionally containing at least one additional heteroatom selected from N, O, S, and P;

each R^4 is independently selected from R^3 , $-SO_2R^3$, $-SO_2N(R^3)R^3$, $-CO_2R^3$, $-C(O)N(R^3)R^3$, and $-C(O)R^3$;

Y is selected from -CH₂-, -O-, -S(O)₀₋₂-, -N(\mathbb{R}^3)-, and absent;

L is selected from $-(CH_2)_{1-3}$, $-(CH_2)_{1-3}N(R^3)$ -, $-(CH_2)_{1-3}O$ -, $-(CH_2)_{1-3}S(O)_{0-2}$ - and absent; each of the aforementioned methylenes optionally substituted;

Z is a five- to seven-membered ring system or -R³, said five- to seven-membered ring system optionally substituted with zero to four of R⁵; and

 R^5 is selected from -H, halogen, -CN, oxo, -NO₂, -OR³, -N(R³)R⁴, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally

substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; and optionally two of R^5 , together with the atoms to which they are attached, form a second ring system fused with said five- to seven-membered ring system, said second ring system substituted with zero to four of R^5 .

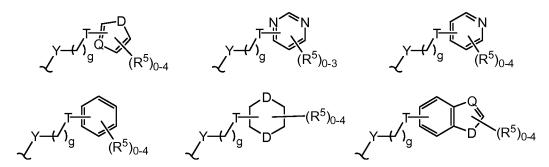
2. (Original) The compound according to claim 1, of formula II,

II

wherein, A and E are each independently N or $-C(R^1)$ -; and G is selected from $-S(O)_{0-2}$ -, and $-C(R^1)=C(R^1)$ -.

3. The compound according to claim 2, wherein Ar is selected from the following formulae.

4. (Original) The compound according to claim 3, wherein -Y-L-Z is selected from the following formulae,



wherein g is zero to two; D is selected from $-C(R^5)(R^5)$ -, -O-, $-S(O)_{0-2}$ -, and $-N(R^4)$ -; Q is =N- or $-C(R^5)$ -, T is selected from absent, $-N(R^3)$ -, -S- and -O-; and each methylene between Y and T is optionally substituted; provided that when both Y and T are heteroatoms then g must be two.

- 5. (Original) The compound according to claim 4, wherein Y is -O- or optionally substituted -CH₂-.
- 6. (Original) The compound according to claim 5, wherein X is selected from the following formulae.

- 7. (Original) The compound according to claim 6, wherein R^{4a} is selected from $-SO_2R^3$, $-SO_2N(R^3)R^4$, $-CO_2R^3$, $-C(O)N(R^3)R^4$, and $-C(O)R^3$.
- 8. (Original) The compound according to claim 7, wherein each R² is independently selected from -H or optionally substituted lower alkyl.
- 9. (Original) The compound according to claim 8, wherein each R^2 is independently selected from -H, haloalkyl, $-C_{1-6}$ alkyl- $N(R^3)R^3$, $-C_{1-6}$ alkyl- OR^3 , $-C_{1-6}$ alkyl- CO_2R^3 , and $-C_{1-6}$ alkyl- CO_3R^3 .
- 10. (Original) The compound according to claim 9, wherein R^{4a} is $-C(O)N(R^3)R^3$ or $-C(O)R^3$.
- 11. (Original) The compound according to claim 10, wherein -Y-L-Z is selected from the following formulae,

wherein Y, T, and g are as described above.

12. (Original) The compound according to claim 11, wherein g is one or two.

- 13. (Original) The compound according to claim 12, wherein each R^5 is independently selected from -H, halogen, -CN, -NH₂, -NO₂, -OR³, -N(R³)R⁴, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, and optionally substituted lower alkyl.
- 14. (Original) The compound according to claim 13, wherein -Y-L-Z is selected from the following formulae.

$$R^{3}$$
 R^{4b} R^{3} R^{4b} R^{3} R^{4b} R^{5} R

15. (Original) The compound according to claim 14, having formula III,

$$R^{3a}$$
 O $(R^5)_{0-2}$ N R^{3b} R^{4b} R^{4b}

Ш

wherein J is N or CH, and B is =N- or = $C(R^5)$ -.

- 16. (Original) The compound according to claim 15, wherein R^{3a} is selected from optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl.
- 17. (Original) The compound according to claim 16, wherein R^{3a} is selected from optionally substituted aryl and optionally substituted heteroaryl.
- 18. (Original) The compound according to claim 17, wherein R^{3a} is optionally substituted phenyl.
- 19. (Original) The compound according to claim 18, wherein said optionally substituted phenyl is substituted with at least one of halogen, -CN, -CF₃, -NH₂, -NO₂, -OR³, -N(R³)R³,

 $-S(O)_{0-2}R^3, -SO_2N(R^3)R^3, -CO_2R^3, -C(O)N(R^3)R^3, -N(R^3)SO_2R^3, -N(R^3)C(O)R^3, -N(R^3)CO_2R^3, -C(O)R^3, optionally substituted lower alkyl, and optionally substituted aryl.$

- 20. (Original) The compound according to claim 19, wherein said optionally substituted phenyl group is substituted with at least one trifluoromethyl group.
- 21. (Original) The compound according to claim 20, wherein said optionally substituted phenyl group is substituted with at least two trifluoromethyl groups
- 22. (Original) The compound according to claim 19, wherein said optionally substituted phenyl group is substituted with at least one lower alkyl group.
- 23. (Original) The compound according to claim 19, wherein R^{3b} is -H.
- 24. (Original) The compound according to claim 23, wherein R^{4b} is selected from R^3 , -H, $-CO_2R^3$, $-C(O)N(R^3)R^4$, and $-C(O)R^3$.
- 25. (Original) The compound according to claim 24, wherein Ar is according to the formula below.

26. (Original) The compound according to claim 24, wherein Ar is according to the formula below.

27. (Original) The compound according to claim 24, wherein Ar is according to the formula below.

28. (Original) The compound according to claim 24, wherein Ar is according to the formula below.

29. (Original) The compound according to claim 24, wherein Ar is according to the formula below.

30. (Original) A compound for modulating kinase activity of Formula IV,

or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

Ar is selected from the following formulae:

$$\sum_{N=1}^{N} \sum_{(R^1)_{0-2}}^{N} \sum_{(R^1)_{0-4}}^{N} \sum_{(R^1)_{0-3}}^{N} \sum_{(R^1)_{0-3}}^{N} \sum_{(R^1)_{0-4}}^{N}$$

each R^1 is independently selected from -H, halogen, -CN, -NO₂, -OR³, -N(R³)R³, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; optionally two of R¹, together with the atoms to which they are attached, form a first ring system fused with Ar, said first ring system substituted with zero to three additional of R¹;

each R^2 is independently selected from -H, halogen, oxo, -CN, -NH₂, -NO₂, -OR³, -N(R³)R³, -N(R³)R⁵, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³,

-N(R³)CO₂R³, -N(R³)C(O)N(R³)R³, -C(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl;

two of R², together with the atoms to which they are attached, can form an optionally substituted three- to seven-membered ring system;

each R³ is independently selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; or

two of R3, when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl ring, said optionally substituted five- to seven-membered heterocyclyl ring optionally containing at least one additional heteroatom selected from N, O, S, and P;

each R⁴ is independently selected from R³, -SO₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, and $-C(O)R^3$:

Y is selected from optionally substituted - CH_2 -, -O-, -S-, and - $N(R^3)$ -;

L is selected from optionally substituted -CH₂-, -O-, -S-, -N(R³)- and absent;

provided that Y and L are not both heteroatoms;

B is =N- or =C(H)-;

at each instance, R⁵ and R⁶ are independently selected from -H, halogen, -CN, -NO₂, -OR³, $-N(R^3)R^4$, $-S(O)_{0-2}R^3$, $-SO_2N(R^3)R^3$, $-CO_2R^3$, $-C(O)N(R^3)R$, $-N(R^3)SO_2R^3$, $-N(R^3)C(O)R^3$, -N(R³)CO₂R³, -C(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; and

optionally two of R⁵, together with the atoms to which they are attached, form a ring system fused with the ring containing B according to formula IV, said ring system substituted with zero to two additional of R⁵.

31. (Original) The compound according to claim 30, wherein Y is -O- and L is optionally substituted -CH₂-.

> Preliminary Amendment Appl. No.: 10/549,300 Attorney Docket No. 05-934-F January 31, 2007

- 32. (Original) The compound according to claim 31, wherein at least one of R⁶ is optionally substituted lower alkyl.
- 33. (Original) The compound according to claim 32, wherein said at least one optionally substituted lower alkyl is *meta* to the piperazine urea function as depicted in formula **IV**.
- 34. (Original) The compound according to claim 33, wherein R^{4a} is selected from R^3 , -H, $-CO_2R^3$, $-C(O)N(R^3)R^4$, and $-C(O)R^3$.
- 35. (Original) The compound according to claim 34, wherein R^{4a} is selected from -H, $-CO_2R^3$, $-C(O)N(R^3)R^4$, and $-C(O)R^3$.
- 36. (Original) The compound according to claim 35, wherein -Y-L- is -OCH₂-.
- 37. (Original) The compound according to claim 36, wherein Ar is according to the formula below.

38. (Original) The compound according to claim 36, wherein Ar is according to the formula below.

39. (Original) The compound according to claim 36, wherein Ar is according to the formula below.

$$\bigvee_{N}$$

40. (Original) The compound according to claim 36, wherein Ar is according to the formula below.

41. (Original) The compound according to claim 36, wherein Ar is according to the formula below.

42. (Original) The compound according to claim 1, selected from Table 4.

Table 4

	i able 4		
1	N-[(1R,2S)-2-phenylcyclopropyl]-4-{4- [(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	NH N N N N N N N N N N N N N N N N N N	
2	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N	
3	N-[4-chloro-3-(trifluoromethyl)phenyl]- 4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C CI	
4	N-[4-(1-methylethyl)phenyl]-4-{4- [(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N	
5	N-(3-bromophenyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N	

Table 4

6	N-[3-(methylthio)phenyl]-4-{4- [(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N
7	N-(3-ethylphenyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
8	N-(3,5-dimethylphenyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
9	N-[3-trifluoromethylphenyl]-4-{4- [(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
10	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-methylquinolin-4-yl)methyl]oxy}- 1,2,5-thiadiazol-3-yl)piperazine-1- carboxamide	F_3C CF_3 N
11	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[3- (dimethylamino)phenyl]methyl}oxy)- 1,2,5-thiadiazol-3-yl]piperazine-1- carboxamide	F ₃ C CF ₃
12	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- (1H-indol-5-yloxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N O NH N-S' N-S'

Table 4

13	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(3-thienylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F_3C CF_3 N
14	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(2-morpholin-4-ylethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C CF ₃
15	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[2-(1H-imidazol-1-yl)ethyl]oxy}-1,2,5- thiadiazol-3-yl)piperazine-1- carboxamide	O N N N N N N N N N N N N N N N N N N N
16	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(1-methylpiperidin-4-yl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C CF ₃
17	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[4-(methyloxy)phenyl]methyl}oxy)- 1,2,5-thiadiazol-3-yl]piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N
18	4-[4-({[3,4-bis(methyloxy)phenyl]methyl}oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	F_3C CF_3 CF_3
19	4-{4-[(1,3-benzodioxol-5-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	F_3C CF_3 $N-S$ O

Table 4

20	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(furan-3-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F_3C CF_3 N
21	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(tetrahydrofuran-3-ylmethyl)oxy]- 1,2,5-thiadiazol-3-yl}piperazine-1- carboxamide	F_3C CF_3 CF_3
22	N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	F_3C CF_3 CF_3
23	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}-1,4-diazepane-1- carboxamide	F ₃ C CF ₃ N-S
24	1-({[(1S,2R,5S)-5-methyl-2-(1-methylethyl)cyclohexyl]oxy}acetyl)-4- {4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	
25	5-phenyl-N-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)-1,3-oxazole-4-carboxamide	
26	1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}-4-{[3- (trifluoromethyl)phenyl]acetyl}piperazi ne	F ₃ C

Table 4

27	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(piperidin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C CF ₃
28	N-[3,5-bis(trifluoromethyl)phenyl]-N'- [(4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperidin-4- yl)methyl]urea	F_3C CF_3 CF_3 CF_3
29	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(3-pyridin-3-ylpropyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C CF ₃ N-S
30	N-[3,5-bis(trifluoromethyl)phenyl]-4- {1,1-dioxido-4-[(pyridin-4- ylmethyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	CE_3 CE_3 CE_3
31	4-[4-(1-azabicyclo[2.2.2]oct-3-yloxy)- 1,2,5-thiadiazol-3-yl]-N-[3,5- bis(trifluoromethyl)phenyl]piperazine-1- carboxamide	O
32	4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]benzoic acid	F_3 C CF_3 $N-S$ CO_2 H
33	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(piperidin-3-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F_3C CF_3 N

Table 4

34	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(2-pyrrolidin-1-ylethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C CF ₃ N-S N
35	4-{4-[(2-amino-2-methylpropyl)oxy]- 1,2,5-thiadiazol-3-yl}-N-[3,5- bis(trifluoromethyl)phenyl]piperazine-1- carboxamide	HN N N NH ₂ F ₃ C CF ₃ N-S
36	N-[3,5-bis(trifluoromethyl)phenyl]-1- {4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperidine-4- carboxamide	F_3C CF_3 N
37	1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}-N-[3- (trifluoromethyl)phenyl]piperidine-4- carboxamide	HN O N N N N N N N N N N N N N N N N N N
38	N-[3,5-bis(trifluoromethyl)phenyl]-4- {3-[(pyridin-4-ylmethyl)oxy]pyrazin-2- yl}piperazine-1-carboxamide	F_3C CF_3 N
39	4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin- 2-yl}-N-[3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	CF ₃
40	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(2-piperidin-4-ylethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F_3C CF_3 N

Table 4

41	2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
42	1-phenyl-4-{4-[(pyridin-4- ylmethyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine	
43	1-[(4-methylphenyl)methyl]-4-{4- [(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine	N N N N N N N N N N N N N N N N N N N
44	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(pyridin-4-ylmethyl)amino]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	F_3C CF_3 HN N N N N N N N N N
45	4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}-N-[3- (trifluoromethyl)phenyl]-1,4-diazepane- 1-carboxamide	HN N N N N N N N N N N N N N N N N N N
46	2-methyl-1-{[2- (methyloxy)phenyl]carbonyl}-4-{4- [(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine	N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-
47	N-[5-chloro-2-(methyloxy)phenyl]-N'-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)urea	

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Table 4

48	N-[5-methyl-2-(methyloxy)phenyl]-N'- (1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}pyrrolidin-3-yl)urea	
49	N-(1-{4-[(pyridin-4-ylmethyl)oxy]- 1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)- N'-[3-(trifluoromethyl)phenyl]urea	F_3C
50	2-methyl-N-[4-(1-methylethyl)phenyl]- 4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	S, S
51	2-methyl-N-[3-(methylthio)phenyl]-4- {4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	
52	(2R)-N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
53	(2R)-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	CF3 NH

Table 4

54	1-[4-(4-{4-[(pyridin-4-ylmethyl)oxy]- 1,2,5-thiadiazol-3-yl}piperazin-1- yl)phenyl]ethanone	
55	2-(4-{4-[(pyridin-4-ylmethyl)oxy]- 1,2,5-thiadiazol-3-yl}piperazin-1- yl)pyrimidine	
56	1-[2-nitro-4-(trifluoromethyl)phenyl]-4- {4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine	F_3C N
57	(2S)-N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	F_3C N
58	(2S)-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	HN—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—N—
59	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3-hydroxypyrazin-2-yl)piperazine-1-carboxamide	N HN CF ₃ CF ₃ CF ₃

Table 4

60	2-[2,5-bis(trifluoromethyl)phenyl]-N-(1- {4-[(pyridin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}pyrrolidin-3- yl)acetamide	F ₃ C O N N N S N
61	1-{[2,5-bis(trifluoromethyl)phenyl]acetyl}-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	F_3C N
62	N-[3,5-bis(trifluoromethyl)phenyl]-2- methyl-4-{3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}piperazine- 1-carboxamide	F_3C CF_3 CF_3
63	2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
64	N-[3,5-bis(trifluoromethyl)phenyl]-2,6-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
65	2,6-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
66	N-(1-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}pyrrolidin-3-yl)-N'-[3-(trifluoromethyl)phenyl]urea	F ₃ C

Table 4

67	N-[3,5-bis(trifluoromethyl)phenyl]-N'-(1-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}pyrrolidin-3-yl)urea	F_3C CF_3
68	N-[3,5-bis(trifluoromethyl)phenyl]-2,6-dimethyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
69	2,6-dimethyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
70	N-[3,5-bis(trifluoromethyl)phenyl]-3- methyl-4-{3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}piperazine- 1-carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
71	3-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	F ₃ C NH NN
72	N-[3,5-bis(trifluoromethyl)phenyl]-4- {2-[(pyridin-4- ylmethyl)oxy]phenyl}piperazine-1- carboxamide	F_3C N

Table 4

	1 able 4		
73	4-{2-[(pyridin-4-ylmethyl)oxy]phenyl}- N-[3- (trifluoromethyl)phenyl]piperazine-1- carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N	
74	N-[3,5-bis(trifluoromethyl)phenyl]-2- methyl-4-{3-[(pyridin-4- ylmethyl)oxy]quinoxalin-2- yl}piperazine-1-carboxamide	HN—CF ₃ CF ₃ CF ₃	
75	N-[3,5-bis(trifluoromethyl)phenyl]-4- {3-[(pyridin-4-ylmethyl)oxy]pyrazin-2- yl}-1,4-diazepane-1-carboxamide	F_3C N	
76	2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]quinoxalin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	N—N—N—N—O CF ₃	
77	4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin- 2-yl}-N-[3-(trifluoromethyl)phenyl]- 1,4-diazepane-1-carboxamide	F_3C N	
78	N-[3,5-bis(trifluoromethyl)phenyl]-2,5-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	F ₃ C NH N N N N N N N N N N N N N N N N N N	
79	2,5-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	CF ₃	

Table 4

80	(2S)-N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	F_3C $\downarrow \qquad \qquad$
81	(2S)-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	F ₃ C N N N N N N N N N N N N N N N N N N N
82	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-fluoropyridin-4-yl)methyl]oxy}- 1,2,5-thiadiazol-3-yl)piperazine-1- carboxamide	F_3C N
83	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-chloropyridin-4-yl)methyl]oxy}- 1,2,5-thiadiazol-3-yl)piperazine-1- carboxamide	F_3C O N
84	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3- {[(2-chloropyridin-4- yl)methyl]oxy}pyrazin-2-yl)piperazine- 1-carboxamide	F_3C N
85	N-[3,5-bis(trifluoromethyl)phenyl]-4-(2- {[(2,3,5,6-tetrafluoropyridin-4- yl)amino]methyl}phenyl)piperazine-1- carboxamide	HN F CF3

Table 4

86	N-[3,5-bis(trifluoromethyl)phenyl]-4-(2- {[(3-chloro-2,5,6-trifluoropyridin-4- yl)amino]methyl}phenyl)piperazine-1- carboxamide	$F \downarrow CI \qquad CF_3$ $F \downarrow CI \qquad CF_3$
87	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-bromopyridin-4-yl)methyl]oxy}- 1,2,5-thiadiazol-3-yl)piperazine-1- carboxamide	F_3C O N
88	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3- {[(2-bromopyridin-4- yl)methyl]oxy}pyrazin-2-yl)piperazine- 1-carboxamide	F_3C P
89	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3- {[(2-fluoropyridin-4- yl)methyl]oxy}pyrazin-2-yl)piperazine- 1-carboxamide	F ₃ C P ₃ C P ₂ C P ₃ C P ₃ C P ₄ C P ₅ C
90	N-[3,5-bis(trifluoromethyl)phenyl]-4- {5,6-dicyano-3-[(pyridin-4- ylmethyl)oxy]pyrazin-2-yl}piperazine- 1-carboxamide	NC N N N O CF3

Table 4

91	4-{5,6-dicyano-3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	NC N N N CF3
92	N-(3-ethylphenyl)-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	$\left\langle \begin{array}{c} z \\ \\ - \overline{z} \\ \\ - \overline{z} \\ \\ - \overline{z} \\ -$
93	N-(3-ethylphenyl)-2-methyl-4-{3- [(pyridin-4-ylmethyl)oxy]pyrazin-2- yl}piperazine-1-carboxamide	
94	N-(3-ethylphenyl)-2,6-dimethyl-4-{3- [(pyridin-4-ylmethyl)oxy]pyrazin-2- yl}piperazine-1-carboxamide	
95	N-(3-ethylphenyl)-2-methyl-4-{3- [(pyridin-4-ylmethyl)oxy]quinoxalin-2- yl}piperazine-1-carboxamide	
96	N-[3,5-bis(trifluoromethyl)phenyl]-4-[3- (2-pyridin-4-ylethyl)pyrazin-2- yl]piperazine-1-carboxamide	$F_{3}C$ CF_{3} N

Table 4

	1 able 4	
97	N-[3,5-bis(trifluoromethyl)phenyl]-4- {3-[(pyridin-4-ylmethyl)oxy]pyridin-2- yl}piperazine-1-carboxamide	F_3C CF_3
98	N-[3,5-bis(trifluoromethyl)phenyl]-4- {2-[(pyridin-4- yloxy)methyl]phenyl}piperazine-1- carboxamide	F_3C CF_3
99	4-(4-{[(2-aminopyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	F_3C CF_3 N
100	1,1-dimethylethyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	HN N N N N N N N N N N N N N N N N N N
101	methyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	F ₃ C CF ₃
102	4-{[(4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-amine	H ₂ N N N N N N N N N N N N N N N N N N N

Table 4

103	N-(4-chlorophenyl)-4-{3-[(pyridin-4-ylmethyl)oxy]pyridin-2-yl}piperazine-1-carboxamide	
104	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
105	N-(3-chlorophenyl)-4-{3-[(pyridin-4-ylmethyl)oxy]pyridin-2-yl}piperazine-1-carboxamide	
106	4-{[(4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}-N-propylpyridin-2-amine	S Z Z HN
107	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(propylamino)pyridin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HZ CF ₃ CCF ₃
108	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(methylamino)pyrimidin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	F ₃ C CF ₃

86

Table 4

109	N-methyl-4-{[(4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-amine	Z-0 Z-0 Z Z
110	N-ethyl-4-{[(4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-amine	Z-0 Z-0 Z-0 Z-0
111	N-butyl-4-{[(4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-amine	Z-S Z-S Z-S
112	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(methylamino)pyridin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HZ CF ₃ CCF ₃
113	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(ethylamino)pyridin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HZ CF ₃ C

Table 4

	Table 4		
114	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(butylamino)pyridin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	F ₃ C CF ₃	
115	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2-[(phenylmethyl)amino]pyridin- 4-yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	F ₃ C CF ₃	
116	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2-[(1- methylethyl)amino]pyrimidin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	F ₃ C CF ₃	
117	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2- [(phenylmethyl)amino]pyrimidin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	F ₃ C CF ₃	
118	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(phenylamino)pyrimidin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N	

Table 4

119	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-{[2- (dimethylamino)ethyl]amino}pyrimidin- 4-yl)methyl]oxy}-1,2,5-thiadiazol-3- yl)piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
120	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-{[2- (dimethylamino)ethyl]amino}pyridin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3- yl)piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
121	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(ethylamino)pyrimidin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	F ₃ C CF ₃
122	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(propylamino)pyrimidin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	F ₃ C CF ₃
123	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(cyclopropylamino)pyrimidin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N

Table 4

124	4-[4-({[2-(acetylamino)pyrimidin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	F ₃ C CF ₃
125	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2- [(phenylcarbonyl)amino]pyridin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	F ₃ C CF ₃
126	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2- [(phenylcarbonyl)amino]pyrimidin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	F ₃ C CF ₃
127	4-{4-[({2- [bis(phenylcarbonyl)amino]pyridin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3-yl}- N-[3,5- bis(trifluoromethyl)phenyl]piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N

Table 4

128	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(cyclopentylamino)pyrimidin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
129	4-[4-({[2-(acetylamino)pyridin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N
130	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2-[({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)amino]pyridin-4-yl}methyl)oxy]- 1,2,5-thiadiazol-3-yl}piperazine-1- carboxamide	F ₃ C HN N N N N N N N N N N N N N N N N N N
131	methyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidin-2-yl}carbamate	HN N N N N N N N N N N N N N N N N N N
132	4-(4-{[(2-aminopyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	NH ₂

Table 4

133	methyl [4-({[4-(4-{[(3-ethylphenyl)amino]carbonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy}methyl)pyridin-2-yl]carbamate	
134	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-cyanopyrimidin-4-yl)methyl]oxy}- 1,2,5-thiadiazol-3-yl)piperazine-1- carboxamide	F ₃ C CF ₃ NC N N N N N N N N N N N N N N N N N N
135	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
136	4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidine-2-carboxamide	H_2N H_2N H_2N H_2N H_3C CF_3
137	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(butyloxy)pyrimidin-4- yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	HN N O N N N N N N N N N N N N N N N N N

Table 4

138	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[(pyrimidin-4-ylmethyl)oxy]-1,2,5- thiadiazol-3-yl}piperazine-1- carboxamide	HN N N N N N N N N N N N N N N N N N N
139	4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridine-2-carboxylicacid	HO N N N S CF3 CF3
140	2-pyrrolidin-1-ylethyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	O N N F ₃ C N N N N N N N N N N N N N N N N N N N
141	2-morpholin-4-ylethyl {4-[({4-[4-(4-[4-(3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	O CF ₃ N F ₃ C N N S N N N N N N N N N N N N N N N N N
142	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N

Table 4

143	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-{[(1-methylpiperidin-3- yl)carbonyl]amino}pyridin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3- yl)piperazine-1-carboxamide	F ₃ C — HN — N — N — N — N — N — N — N — N —
144	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	NH ₂
145	2-(4-methylpiperazin-1-yl)ethyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	O O CF ₃ N NH CF ₃ N NH O NH O N
146	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-{[(1-ethylpiperidin-4- yl)carbonyl]amino}pyridin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3- yl)piperazine-1-carboxamide	HN N N N N N N N N N N N N N N N N N N

Table 4

1 able 4				
147	4-(4-{[(2-aminopyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-{3-[(trifluoromethyl)thio]phenyl}piperazin e-1-carboxamide	NH ₂ S-CF ₃ NH		
148	4-({[4-(4-{[3,5-bis(trifluoromethyl)phenyl]sulfonyl}pip erazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy}methyl)pyridin-2-amine	N-S $N-S$		
149	4-(4-{[(2-aminopyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-naphthalen-1-ylpiperazine-1-carboxamide	NH ₂ NH		
150	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2-[(N,N-dimethylglycyl)amino]pyridin-4-yl}methyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	F ₃ C CF ₃		
151	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2-[(morpholin-4- ylacetyl)amino]pyridin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	F ₃ C CF ₃		

Table 4

152	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2-[(piperidin-1- ylacetyl)amino]pyridin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	F ₃ C CF ₃
153	ethyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	F ₃ C CF ₃
154	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2-[(pyrrolidin-1- ylacetyl)amino]pyridin-4- yl}methyl)oxy]-1,2,5-thiadiazol-3- yl}piperazine-1-carboxamide	F ₃ C CF ₃
155	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4- {[(2-{[(4-methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3- yl)piperazine-1-carboxamide	F ₃ C CF ₃
156	N-[3,5-bis(trifluoromethyl)phenyl]-4- {4-[({2-[(N,N-diethylglycyl)amino]pyridin-4-yl}methyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	F ₃ C CF ₃

Table 4

157	1-ethylpiperidin-4-yl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	F ₃ C CF ₃
158	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	NH ₂
159	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4- ({[2-(2-oxo-1,3-oxazolidin-3-yl)pyridin- 4-yl]methyl}oxy)-1,2,5-thiadiazol-3- yl]piperazine-1-carboxamide	F ₃ C CF ₃
160	2-(diethylamino)ethyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	F ₃ C F ₃ C
161	methyl [4-({[2-(4-{[(3-ethylphenyl)amino]carbonyl}piperazin-1-yl)pyridin-3-yl]oxy}methyl)pyridin-2-yl]carbamate	

Table 4

162	2-pyrrolidin-1-ylethyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidin-2-yl}carbamate	F ₃ C CF ₃
163	2-piperidin-1-ylethyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidin-2-yl}carbamate	OND CF3 N NH CF3 CF3 CF3
164	methyl [4-({[2-(4-{[(3-bromophenyl)amino]carbonyl}piperazin -1-yl)pyridin-3-yl]oxy}methyl)pyridin-2-yl]carbamate	Br N N N N N N N N N N N N N N N N N N N
165	methyl {4-[({2-[4-({[3-(methyloxy)phenyl]amino}carbonyl)piperazin-1-yl]pyridin-3-yl}oxy)methyl]pyridin-2-yl}carbamate	
166	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-(methyloxy)phenyl]piperazine-1-carboxamide	

Table 4

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167	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-(1-methylethyl)phenyl]piperazine-1-carboxamide	NH ₂ N N N N N N N N N N N N N N N N N N N
168	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-{3-[(trifluoromethyl)oxy]phenyl}piperazine -1-carboxamide	NH ₂ N N N N N N N N N N N N N N N N N N N
169	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	NH ₂ N N N N N N N N N N N N N N N N N N N
170	N-(3-ethylphenyl)-4-[3-({[2-({[(3-ethylphenyl)amino]carbonyl}amino)pyridin-4-yl]methyl}oxy)pyridin-2-yl]piperazine-1-carboxamide	HN NH NH NH
171	N-(3-ethylphenyl)-4-(3-{[(2-{[(4- methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- 1-carboxamide	NH NH NH

Table 4

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172	N-(3-ethylphenyl)-4-(4-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	N S N N N N N N N N N N N N N N N N N N
173	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3- {[(2-{[(4-methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- 1-carboxamide	N N N N N N N N N N
174	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
175	4-[3-({[2-(acetylamino)pyridin-4-yl]methyl}oxy)pyridin-2-yl]-N-(3-ethylphenyl)piperazine-1-carboxamide	NH NH NH
176	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-ethyl-4-fluorophenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N

Table 4

177	2-[4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)piperazin-1-yl]-N-[3,5-bis(trifluoromethyl)phenyl]acetamide	N N N N N N N N N N N N N N N N N N N
178	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-phenylpiperazine-1-carboxamide	H ₂ N N N NH NH
179	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide	H ₂ N NH NH CI
180	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	H_2N N N N N N N N N N
181	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-bromo-5-ethylphenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N

Table 4

182	2-(4-methylpiperazin-1-yl)ethyl [4-({[2-(4-{[(3-ethylphenyl)amino]carbonyl}piperazin-1-yl)pyridin-3-yl]oxy}methyl)pyridin-2-yl]carbamate	
183	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-chlorophenyl)piperazine-1-carboxamide	H ₂ N NH NH CI
184	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-bromophenyl)piperazine-1-carboxamide	H ₂ N N N NH NH Br
185	N-[4-({[2-(4-acetylpiperazin-1-yl)pyridin-3-yl]oxy}methyl)pyridin-2-yl]-2-(4-methylpiperazin-1-yl)acetamide	HN N N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
186	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-fluorophenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
187	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(4-fluorophenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N

Table 4

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188	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(2-fluorophenyl)piperazine-1-carboxamide	H_2N N N N N N N N N N
189	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide	H ₂ N NH NH
190	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-5-bromopyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	Br N N N N N N N N N N N N N N N N N N N
191	N-methyl-4-(3-{[(2-{[(4- methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- 1-carboxamide	N N N N N N N N N N N N N N N N N N N
192	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[2-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
193	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(5-chloro-2-fluorophenyl)piperazine-1-carboxamide	H ₂ N NH NH NH
194	4-(3-{[(2-amino-5-bromopyrimidin-4-yl)methyl]oxy}-5-bromopyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	Br N N N N N N N N N N N N N N N N N N N

Table 4

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195	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[2-fluoro-3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
196	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H ₂ N NH NH CF ₃
197	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide	H ₂ N NH NH CI
198	N-(3-chloro-5-ethylphenyl)-4-(3-{[(2- {[(4-methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- 1-carboxamide	NH NH NH CI
199	N-(5-ethyl-2-fluorophenyl)-4-(3-{[(2- {[(4-methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- 1-carboxamide	N N N N N N N N N N N N N N N N N N N
200	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-ethyl-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H ₂ N NH NH CF ₃

Table 4

201	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
202	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide	H ₂ N N NH CI
203	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
204	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-methylpiperazine-1-carboxamide	H_2N N N N N N N N N N
205	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-ethylpiperazine-1-carboxamide	H_2N N N N N N N N N N
206	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-cyclohexylpiperazine-1-carboxamide	H ₂ N NH NH
207	4-({[2-(4-acetylpiperazin-1-yl)pyridin-3-yl]oxy}methyl)pyrimidin-2-amine	N N N N N N N N N N N N N N N N N N N

Table 4

208	4-({[2-(4-propanoylpiperazin-1-yl)pyridin-3-yl]oxy}methyl)pyrimidin-2-amine	N N N N N N N N N N N N N N N N N N N
209	N-(3-cyclopropylphenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide	
210	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-cyclopropylphenyl)piperazine-1-carboxamide	H ₂ N NH NH
211	N-[2-fluoro-5-(trifluoromethyl)phenyl]- 4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine- 1-carboxamide	N N N N N N N N N N
212	N-[3-fluoro-5-(trifluoromethyl)phenyl]- 4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine- 1-carboxamide	N N N N N N N N N N

Table 4

213	N-(3,5-dichlorophenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide	NH NH NH CI
214	4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	$\begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$
215	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
216	4-(3-{[1-(2-aminopyrimidin-4-yl)ethyl]oxy}pyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
217	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide	H_2N N N N N N N N N N
218	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N

Table 4

219	4-[({2-[4-(3,4-dihydroquinolin-1(2H)-ylcarbonyl)piperazin-1-yl]pyridin-3-yl}oxy)methyl]pyrimidin-2-amine	N NH ₂
220	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(2-methylpropyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
221	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide	O H CI
222	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
223	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide	O H C C C C C C C C C C C C C C C C C C
224	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-phenylpiperazine-1-carboxamide	H ₂ N N N NH
225	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N

Table 4

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226	N-(3,5-diethylphenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)oxy]methyl}pyridin-2-yl)piperazine-1-carboxamide	NH NH NH
227	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-methylpyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	H ₂ N NH NH
228	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-methylpyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
229	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
230	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-phenylpiperazine-1-carboxamide	H ₂ N N N NH
231	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N

Table 4

232	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
233	N-[3-chloro-5-(trifluoromethyl)phenyl]- 4-(3-{[(2-{[(4-methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- 1-carboxamide	P P P P P P P P P P
234	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[3-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
235	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	$\begin{array}{c c} & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$
236	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3-bromo-5-ethylphenyl)piperazine-1-carboxamide	H_2N N N N N N N N N N
237	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-chloropyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	CI N N NH NH

Table 4

238	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-bromo-5-ethylphenyl)piperazine-1-carboxamide	S-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N
239	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
240	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	F_3 C
241	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3-ethyl-4-fluorophenyl)piperazine-1-carboxamide	H ₂ N N N N NH NH
242	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide	S N N N N N N N N N N N N N N N N N N N
243	N-[3-chloro-2-fluoro-5- (trifluoromethyl)phenyl]-4-(3-{[(2-{[(4- methylpiperazin-1- yl)acetyl]amino}pyridin-4- yl)methyl]oxy}pyridin-2-yl)piperazine- 1-carboxamide	N N N N N N N N N N

Table 4

244	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-chloropyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
245	4-(3-{[1-(2-aminopyrimidin-4-yl)ethyl]oxy}pyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
246	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-chloropyridin-2-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	CI N N N N N N N N N N N N N F
247	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-ethyl-5-fluorophenyl)piperazine-1-carboxamide	H ₂ N NH NH
248	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-chloro-2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	F_3C
249	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-chloro-2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N

Table 4

250	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]-N-methylpiperazine-1-carboxamide	H_2N N N N N N N N N N
251	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[3-(1-methylethyl)phenyl]piperazine-1-carboxamide	H ₂ N N N NH
252	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-ethyl-4-fluorophenyl)piperazine-1-carboxamide	H ₂ N N N N N N N N N N N N N N N N N N N
253	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-chloro-4-fluorophenyl)piperazine-1-carboxamide	H ₂ N N N NH
254	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[2,5-bis(methyloxy)phenyl]piperazine-1-carboxamide	N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-
255	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N F_3C CF_3
256	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(3-ethylphenyl)piperazine-1-carboxamide	H ₂ N N NH

Table 4

257	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(5-chloro-2-fluorophenyl)piperazine-1-carboxamide	H_2N N N N N N N N N N
258	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-{3-[(trifluoromethyl)oxy]phenyl}piperazine-1-carboxamide	H_2N N N N N N N N N N
259	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-(methyloxy)phenyl]piperazine-1-carboxamide	H ₂ N NH NH
260	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-ethyl-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
261	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-(1-methylethyl)phenyl]piperazine-1-carboxamide	H ₂ N N NH
262	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[2-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
263	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-fluorophenyl)piperazine-1-carboxamide	H_2N N N N N N N N N N

Table 4

264	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[2-(ethyloxy)phenyl]piperazine-1-carboxamide	H ₂ N NH NH
265	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3,4-difluorophenyl)piperazine-1-carboxamide	H ₂ N NH F
266	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-(methylthio)phenyl]piperazine-1-carboxamide	H ₂ N NH NH
267	N-(3-acetylphenyl)-4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	H ₂ N NH NH
268	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
269	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(3-fluorophenyl)piperazine-1-carboxamide	H ₂ N NH
270	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-phenylpiperazine-1-carboxamide	H ₂ N NH NH

Table 4

271	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide	H_2N N N N N N N N N N
272	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
273	4-[4-({[6,7-bis(methyloxy)quinolin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	F ₃ C CF ₃
274	4-({[4-(4-{[3,5-bis(trifluoromethyl)phenyl]acetyl}piper azin-1-yl)-1,2,5-thiadiazol-3-yl]oxy}methyl)pyrimidin-2-amine	F_3 C F_3
275	5-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]pyrazine-2-carboxamide	H_2N N N N N N N N N N

Table 4

276	4-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	F ₃ C CF ₃
277	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-[3-ethyl-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	H_2N N N N N N N N N N
278	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	H ₂ N NH NH
279	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide	H ₂ N NH NH
280	4-[({4-[4-(naphthalen-2-ylacetyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidin-2-amine	S-N-N-N-O N-N-O
281	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide	H ₂ N NH NH CI

43. (Original) A pharmaceutical composition comprising the compound according to any one of claims 1 - 42 and a pharmaceutically acceptable carrier.

44. (Currently Amended) A metabolite of the compound or the pharmaceutical composition

according to any one of claims 1 - 4342.

45. (Currently Amended) A method of modulating the *in vivo* activity of a kinase, the method

comprising administering to a subject an effective amount of a composition comprising at least

one of the compound according to any of claims 1 - 42-and the pharmaceutical composition

according to claim 43.

46. (Original) The method according to claim 45, wherein the kinase is Tie-2.

47. (Original) The method according to claim 46, wherein modulating the *in vivo* activity of

Tie-2 comprises inhibition of Tie-2.

48. (Currently Amended) A method of treating diseases or disorders associated with

uncontrolled, abnormal, and/or unwanted cellular activities, the method comprising

administering, to a mammal in need thereof, a therapeutically effective amount of a composition

comprising at least one of the compound according to any of claims 1 - 42 and the

pharmaceutical composition according to claim 43.

49. (Currently Amended) A method of screening for modulator of a Tie-2 kinase, the method

comprising combining either a composition comprising at least one of the compound according

to any of claims 1 - 42 and the pharmaceutical composition according to claim 43, and at least

one candidate agent and determining the effect of the candidate agent on the activity of said

kinase.

50. (Currently Amended) A method of inhibiting proliferative activity in a cell, the method

comprising administering to said cell an effective amount of at least one of the compound

according to any of claims 1 - 42-and the pharmaceutical composition according to claim 43.

51. (New) A metabolite of the pharmaceutical composition according to claim 43.

52. (New) A method of modulating the *in vivo* activity of a kinase, the method comprising

administering to a subject an effective amount of a pharmaceutical composition according claim

43.

53. (New) The method according to claim 52, wherein the kinase is Tie-2.

Preliminary Amendment Appl. No.: 10/549,300 54. (New) The method according to claim 53, wherein modulating the *in vivo* activity of Tie-

2 comprises inhibition of Tie-2.

55. (New) A method of treating diseases or disorders associated with uncontrolled, abnormal,

and/or unwanted cellular activities, the method comprising administering, to a mammal in need

thereof, a therapeutically effective amount of a pharmaceutical composition according to claim

43.

56. (New) A method of screening for modulator of a Tie-2 kinase, the method comprising

combining a pharmaceutical composition according to claim 43, and at least one candidate agent

and determining the effect of the candidate agent on the activity of said kinase.

57. (New) A method of inhibiting proliferative activity in a cell, the method comprising

administering to said cell an effective amount of the pharmaceutical composition according to

claim 43.

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